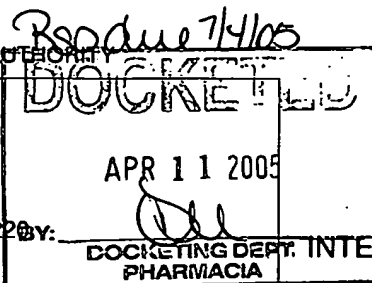


# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY



# PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/IB2004/004187

International filing date (day/month/year)  
15.12.2004

Priority date (day/month/year)  
19.12.2003

International Patent Classification (IPC) or both national classification and IPC  
C07D401/14, A61K31/495, A61P29/00

Applicant  
PHARMACIA CORPORATION

## 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

## 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

## 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/IB2004/004187

iAP20 Rec'd PCT/PTO 19 JUN 2006

**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,  
☒ claims Nos. 12-13

because:

- ☒ the said international application, or the said claims Nos. 12-13 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- |                            |  |
|----------------------------|--|
| the written form           | <input type="checkbox"/> has not been furnished            |
|                            | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished            |
|                            | <input type="checkbox"/> does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/IB2004/004187

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or  
industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	1-13
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-13
Industrial applicability (IA)	Yes: Claims	1-11
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

**WRITTEN OPINION OF THE  
 INTERNATIONAL SEARCHING  
 AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/IB2004/004187

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 12-13 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(i) PCT).

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

D1: WO A 03/104223

The present application relates to a crystalline form of 2-{4-[3-(4-chloro-2-fluorophenyl)-4-pyrimidin-4-yl-1H-pyrazol-5-yl]piperidin-1-yl}-2-oxoethanol (claims 1-5), pharmaceutical compositions thereof (claims 6-11) and a method of treatment by administering the above compound (claims 12-13).

For the assessment of the present claims 12-13 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

The obviously amorphous form of 2-{4-[3-(4-chloro-2-fluorophenyl)-4-pyrimidin-4-yl-1H-pyrazol-5-yl]piperidin-1-yl}-2-oxoethanol is known from ex. 27 according to D1. The crystalline form of this substance is not known.

The subject-matter of claims 1-13 according to the present case is therefore novel in the sense of Article 33(2) PCT.

Closest prior art is D1

To be inventive a chemical compound should

- a. possess a structure that is unexpected
- b. exhibit a use or an effect which is unexpected (Guidelines C-IV, 9.10)
- c. the compound has been prepared by an inventive process, but only in the case where a technical prejudice to its production or unsurmountable difficulties in its production were believed to exist (Guidelines C-IV, 9.8(d) )

None of the above requirements are fulfilled in the present case.

An inventive step in the sense of Article 33(3) PCT cannot be acknowledged for the subject-matter of claims 1-13, unless a surprising effect is demonstrated which would serve to distinguish the crystalline form of 2-{4-[3-(4-chloro-2-fluorophenyl)-4-pyrimidin-4-yl-1H-pyrazol-5-yl]piperidin-1-yl}-2-oxoethanol further from its amorphous form disclosed in ex. 27 of D1.

Further objections:

The term "about" used throughout the claims is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).